IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Kemmerer, Elizabeth
BAKER, et al.	Art Unit: 1646
Application Serial No. 09/991,150	Confirmation No: 4272
Filed: November 16, 2001	Attorney's Docket No. 39780-2730 P1C48
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	**Customer No. 35489**

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ON APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPELLANTS' BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

This Appeal Brief, filed in connection with the above captioned patent application, is responsive to the Final Office Action mailed on September 16, 2004. A Notice of Appeal was filed herein on January 27, 2005. A request for a four month extension of time is filed concurrently herewith. Appellants hereby appeal to the Board of Patent Appeals and Interferences from the final rejection in this case.

The Commissioner is authorized to charge any fees which may be required, including extension fees, or credit any overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2730 P1C48**.

The following constitutes the Appellants' Brief on Appeal.

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I. REAL PARTY IN INTEREST

The real party in interest is Genentech, Inc., South San Francisco, California, by an assignment of the parent application, U.S. Serial No. 09/941,992 recorded November 16, 2001, at Reel 012176 and Frame 0450.

II. RELATED APPEALS AND INTERFERENCES

The claims pending in the current application are directed to nucleic acids encoding PRO341 polypeptides. There exist two related patent applications, (1) U.S. Serial No. 09/941,992, filed August 28, 2001 (containing claims directed to PRO341 polypeptides), and, (2) U.S. Serial No. 09/990,711, filed November 14, 2001 (containing claims directed to antibodies to the PRO341 polypeptide). These two related applications are also under final rejection from the same Examiner and based upon the same outstanding rejection, therefore appeal of these final rejections are being pursued independently and concurrently herewith.

III. STATUS OF CLAIMS

The current application was filed with Claims 1-118. In a Preliminary Amendment filed on November 16, 2001, Appellants canceled Claims 1-118 and added new claims 119-138. In an Amendment filed on January 7, 2004, Claims 119-123, 127-128 and 132-134 were canceled and Claim 124 was amended. A Request for Continued Examination was filed July 7, 2004 in response to a Final Office Action dated March 3, 2004 wherein Claims 139-145 were added and the pending claims were further amended for clarity. A second final rejection was mailed September 16, 2004 and a Notice of Appeal was filed on January 12, 2005. In Amendment after Final, filed December 21, 2004, Claim 124 was amended to remove references to polypeptides, Claims 125-128 were canceled and Claim 139 was amended to clearly recite that "at least a 30 nucleotide fragment of the nucleic acid sequence of SEQ ID NO: 19, or a complement thereof, hybridizes specifically to SEQ ID NO: 19 under well-defined hybridization conditions". An Advisory Action was mailed January 14, 2005. Claims 124, 129-131 and 135-145 remain pending and under final rejection, wherein the rejection of these claims is being appealed herein.

A copy of the rejected claims in the present Appeal is provided as Appendix A.

IV. STATUS OF AMENDMENTS

The amendments in the response after Final, filed on December 21, 2004 were entered for purposes of this appeal, as indicated in the Advisory action mailed January 14, 2005. Further, the request filed under Rule C.F.R. §1.48 for correction of inventorship, filed on January 27, 2005 has also been entered (as determined by PAIR) for purposes of this appeal.

V. SUMMARY OF INVENTION

Independent Claim 124 is directed to an isolated nucleic acid of SEQ ID NO: 20 which encodes for the PRO341 polypeptide. The PRO341 gene was shown for the first time in the present patent application to be significantly amplified in human lung cell carcinomas as compared to normal, non-cancerous human tissue controls. Example 170 at page 539, line 19, to page 555, line 5, sets forth a 'Gene Amplification assay' which shows that the PRO341 gene is amplified in the genome of certain human lung cancers (specifically, see Table 9A, page 550, third column). The profiles of various primary lung tumors used for screening the PRO polypeptide compounds of the invention in the gene amplification assay are summarized on Table 8, page 546 of the specification. This feature is specifically recited in claim 124, and carried by all claims dependent from claim 124. Pending Claims 129-131 depend from Claim 124. The amino acid sequence of the native "PRO341" polypeptide and the nucleic acid sequence encoding this polypeptide (referred to in the present application as "DNA26288-1239") are shown in the present specification as SEQ ID NOs: 20 and 19, respectively, and in Figures 12 and 11, respectively. Page 288, lines 14-17 of the specification provides the description for Figures 12 and 11. The cDNA for PRO341 was deposited under ATCC accession number 209792.

Independent Claim 135 is directed to an isolated nucleic acid consisting of at least 30 nucleotide fragment of the nucleic acid sequence of SEQ ID NO: 19, or a complement thereof, that specifically hybridizes under stringent conditions to (a) the nucleic acid sequence of SEQ ID NO: 19 or a complement thereof; or (b) the full-length coding sequence of the cDNA deposited under ATCC accession number 209792 or a complement thereof and wherein the isolated nucleic acid molecule is suitable for use as a PCR primer or probe. Support for the high stringent hybridization conditions are provided on page 312, line 33 onwards; support for probes of varying lengths is provided on page 285, line 11 onwards. Pending Claims 140-145 depend

from Claim 139 and recite probes consisting of nucleotide fragments of varying lengths; for example, at least 50 nucleotides (Claim 140), 60 nucleotides (Claim 141), 70 nucleotides (Claim 142), 80 nucleotides (Claim 143), 90 nucleotides (Claim 144) and 100 nucleotides (Claim 145).

VI. ISSUES BEFORE THE BOARD

1. Whether Claims 124, 129-131 and 135-145 satisfy the utility requirement under 35 U.S.C. §101.

2. Whether Claims 124, 129-131 and 135-145 satisfy the enablement requirement under 35 U.S.C. §112, first paragraph.

VII. GROUPING OF CLAIMS

For the purposes of this appeal, all claims (Claims 124, 129-131 and 135-145) stand and fall together.

VIII. ARGUMENTS

Summary of the Arguments

Issue 1: Utility

Claims 124-126 and 129-131 and 135-145 stand rejected under 35 U.S.C. §101 as allegedly lacking either a specific and substantial asserted utility or a well established utility. Applicants submit that the gene encoding PRO341 of SEQ ID No: 19 has patentable utility based on the gene amplification data shown in Example 170 of the instant specification. The gene encoding PRO341 showed significant amplification, ranging from 2.173 to 2.514 fold in three different lung primary tumors. Appellants have also submitted with their Response filed July 7, 2004, the Declaration of Dr. Audrey Goddard, which explains that a gene identified as being amplified at least 2-fold by the disclosed gene amplification assay, in a tumor sample, relative to a normal sample, is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy. Therefore, one of ordinary skill would find it credible that the claimed PRO341 gene has utility as a marker for the diagnosis of lung tumors.

However, the Examiner asserted on Page 3 of the Final Office Action mailed September 16, 2004 that "(t)he specification indicates that the PRO341 gene is amplified in only 3 out of 14

lung tumor samples." The Examiner adds that "the literature reports that lung epithelium is at risk for cellular damage.....which result in aneuploidy before the epithelial cells turn cancerous" and cites the reference Hittelman for support. In the Advisory Action dated January 14, 2005, the Examiner adds (on page 2) that "the gene amplification assay (i)n the specification does not provide a comparison between the lung tumor samples and normal lung epithelium, and thus it is not clear that the PRO341 gene is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium."

Appellants submit that, in fact the Hittelman reference cited by the Examiner supports the Appellants position that there is utility in identifying genetic biomarkers in epithelial tissues at cancer risk (see Hittelman, abstract, line 4-7). Appellants had previously submitted that even if PRO341 detects precancerous cells, PRO341 is still a precancer marker and therefore has utility. As one skilled in the art would clearly know, early detection of lung cancer provides information in advance about risk assessment, prognosis and therapy for lung cancer.

Accordingly, Appellants submit that when the proper legal standard is applied, one should reach the conclusion that the present application discloses at least one patentable utility for the claimed PRO341 gene.

Issue 2: Enablement

Claims 124, 129-131 and 135-145 stand rejected under 35 U.S.C. §112, first paragraph, allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." (the Final Office Action mailed September 16, 2004).

Appellants submit that, as discussed above, the PRO341 gene has utility in the diagnosis of lung cancer. Based on such a utility, the teachings in the art and in the specification, one of skill in the art would know exactly how to use the claimed polypeptides for the diagnosis of cancer, without any undue experimentation.

Response to Rejections:

Issue 1. Claims 124, 129-131 and 135-145 are supported by a credible, specific and substantial asserted utility, and thus meet the utility requirement of 35 U.S.C. § 101

The sole basis for the Examiner's rejection of claim 124, 129-131 and 135-145 under this section is that the data presented in Example 170 of the present specification is allegedly insufficient under the present legal standards to establish a patentable utility under 35 U.S.C. § 101 for the presently claimed subject matter. Appellants strongly disagree and, therefore, respectfully traverse the rejection.

A. The Legal Standard For Utility Under 35 U.S.C. § 101

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001), an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility".

Under the Utility Guidelines, an asserted utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a particular composition of matter is useful in general as a diagnostic tool, without also identifying the particular condition that is to be diagnosed using that diagnostic tool. However, when the condition that is capable of being diagnosed is specifically identified and linked to the claimed subject matter, the asserted utility satisfies the "specificity" requirement.

The requirement of a "substantial" utility defines a "real world" use, and derives from the U.S. Supreme Court's holding in Brenner v. Manson, 383 U.S. 519, 534 (1966) stating that:

> "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility."

In explaining the "substantial" utility standard, the Manual of Patent Examining Procedure (MPEP) § 2107.01 cautions, however, that Patent Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient" (MPEP § 2107.01, emphasis supplied). Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in MPEP § 2107 II(B)(1) gives the following instruction to patent examiners:

> "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility". (Emphasis supplied).

Moreover, the Utility Guidelines make clear that the requirement for the asserted utility be "substantial" arises solely for the purpose of excluding:

> "'throw-away' or 'insubstantial'.....utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. § 101". (66 Fed. Reg. 1092, 1098 (2001), emphasis supplied).

Finally, the Utility Guidelines also restate the Patent Office's long established position that any asserted utility must be "credible". "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the applicant's assertions." (MPEP § 2107 II(B)(1)(ii)). According to the Revised Interim Utility Guidelines Training Materials published by the U.S. Patent Office in 1999, Office personnel must always accept a patent applicant's assertion of utility as "credible" unless (1) the logic underlying the assertion is "seriously flawed", or (ii) if the facts upon which the assertion of utility is based are "inconsistent with the logic underlying the assertion".

Moreover, the U.S. Patent Office also sets forth the evidentiary standard as to utility rejections under 35 U.S.C. § 101. In general, an Applicant's assertion of utility creates a presumption of utility that is sufficient to satisfy the utility requirement of 35 U.S.C. § 101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." In re Langer, 503 F.2d 1380, 1391 (CCPA 1974). See, also In re Jolles, 628 F.2d 1322 (CCPA 1980); In re Irons, 340 F.2d 974 (CCPA 1965); In re Sichert, 566 F.2d 1154, 1159 (CCPA 1977). Compliance with 35 U.S.C. § 101 is a question of fact. Raytheon v. Roper, 724 F.2d 951, 956 (Fed. Cir. 1983) cert. denied, 469 U.S. 835 (1984). The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. In re Oetiker, 977 F.2d 1443, 1445 (Fed. Cir. 1992). Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility. Absolute predictability

is not a requirement. Only after the Examiner makes a proper *prima facie* showing under this standard does the burden of rebuttal shift to the patent applicant.

B. The Data and Documentary Evidence Supporting a Patentable Utility

The data presented by the Appellants in the present application and which underlies the current dispute is presented in Example 170 starting on page 539 of the specification. Example 170 describes the results obtained using a very well-known and routinely employed polymerase chain reaction (PCR)-based assay, the TaqMan PCR assay, also referred to herein as the gene amplification assay. This assay allows one to quantitatively measure the level of gene amplification in a given sample, say, a tumor extract, or a cell line. It was well known in the art at the time the invention was made that gene amplification is an essential mechanism for oncogene activation. Appellants isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 9A (pages 539 onwards of the specification), including primary lung cancers of the type and stage indicated in Table 8 (page 546). The tumor samples were tested in triplicates with Taqman™ primers and with internal controls, beta-actin and GADPH in order to quantitatively compare DNA levels between samples (page 548, lines 33-34). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 539, lines 27-29) and also, no-template controls (page 548, lines 33-34). The results of TaqMan™ PCR are reported in ΔCt units, as explained in the passage on page 539, lines 37-39. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold amplification and so on . Using this PCR-based assay, Appellants showed that the gene encoding for PRO341 was significantly amplified, that is, it showed approximately 1.12-1.33 ΔCt units which corresponds to $2^{1.12}$ -$2^{1.33}$- fold amplification or 2.173 fold to 2.514-fold amplification in three lung tumors.

In support of their showing that these gene amplification values are significant, Appellants submitted, in their Response filed July 7, 2004, a Declaration by Dr. Audrey Goddard. Appellants particularly draw the Board's attention to page 3 of the Goddard Declaration which clearly states that:

> It is further my considered scientific opinion that an at least **2-fold increase** in gene copy number in a tumor tissue sample relative to a normal (*i.e.,* non-tumor) sample is significant and useful in that the detected increase in gene copy number in the tumor

> sample relative to the normal sample serves as a basis for using relative gene copy number as quantitated by the TaqMan PCR technique as a diagnostic marker for the presence or absence of tumor in a tissue sample of unknown pathology. Accordingly, a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is **useful as a marker for the diagnosis of cancer**, for monitoring cancer development and/or for measuring the efficacy of cancer therapy. (Emphasis added).

Accordingly, the 2.173-fold to 2.514-fold amplification observed for PRO314 in the three lung tumors would be considered significant and credible by one skilled in the art, based upon the facts disclosed in the Goddard Declaration.

It is also well known that gene amplification occurs in most solid tumors, which includes lung carcinomas, and is generally associated with poor prognosis. Therefore, the PRO314 gene becomes an important diagnostic marker to identify such malignant lung carcinomas, even if the lung malignancy associated with PRO314 molecule is a rare occurrence. Accordingly, the present specification clearly discloses evidence that the gene encoding the PRO314 polypeptide is significantly amplified in certain types of lung carcinoma tumors and therefore is, a valuable diagnostic marker for identifying certain types of lung carcinomas.

Contrary to the Appellants assertion of utility, however, the Examiner alleges that the gene amplification results presented in Example 170 do not render the presently claimed genes patentably useful, and, finds the declaratory evidence presented in this case, "non-persuasive". Appellants respectfully submit, however, that upon application of the proper legal standards described above, the appropriate conclusion is that the present application does, in fact, disclose at least one patentable utility for the claimed PRO314 gene.

C. Proper Legal Analysis of the Data and Documentary Evidence

Appellants respectfully submit that the data presented in Example 170 of the specification and the cumulative evidence of record support a "specific, substantial and credible" asserted utility for the presently claimed invention.

(i) and (ii) The Requirements For "Specific" and "Credible" Utility

The requirements as set forth in the above described Utility Guidelines under 35 U.S.C. § 101 is that an asserted utility for a claimed invention must be "specific" and "credible".

Appellants have clearly demonstrated that the nucleic acid encoding the PRO341 polypeptide of SEQ ID NO: 20 is detectably amplified in certain cancerous human lung tumors.

In this regard, on page 3 of the Office Action of the Final Office Action mailed on September 16, 2004, the Examiner says :

> "the rejection does not question the presumption of truth, or credibility of the asserted utility. The asserted utilities of cancer diagnostics and cancer therapeutics for the claimed nucleic acids are credible and specific" (emphasis added).

Therefore, Appellants respectfully submit, and the Examiner agrees, that the present invention clearly satisfies the "specificity" and "credible" requirement.

(iii) The Requirement For A "Substantial" Utility

As described above, a third requirement set forth in the Utility Guidelines is that an asserted utility for a claimed invention must be "substantial", meaning that the claimed invention must serve a "practical purpose" (see MPEP § 2107 II(B)(1)) which is not a "throw-away or insubstantial [use], such as the use of a complex invention as landfill. (66 Fed. Reg. 1092, 1098 (2001), emphasis supplied).

a) *Appellants have provided a "reasonable use" for the invention which is sufficient to satisfy the requirements of "substantial utility"*

Appellants note that on page 3 of the Final Office Action mailed on September 16, 2004, the Examiner states:

> "... (the asserted utilities) are not substantial. The data set forth in the specification are preliminary at best..... an asserted utility must exist in currently available form." (emphasis added).

First of all, MPEP § 2107.01 cautions the Patent Office personnel to be careful not to interpret the phrase "immediate benefit to the public" or similar formulations, used in certain court decisions, to mean that, products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. In this instance, the Examiner has done just that and interpreted the "substantial utility" requirement to mean that "an asserted utility must exist in currently available form," which is legally incorrect. In fact, MPEP

§ 2107.01 adds that, "(r)ather, **any reasonable use** that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient" (emphasis supplied). Appellants have clearly demonstrated at least one "reasonable use" for the PRO341 polypeptide, that is, as a diagnostic marker for detecting or at least classifying lung carcinomas. Such uses of the claimed invention serve a "practical purpose", which is not a "throw-away or insubstantial [use], such as the use of a complex invention as landfill." That is, Appellants have for the first time identified a particular human gene, the PRO341 gene, that is differentially amplified in certain types of cancerous human lung tumors and this discovery provides for the first time, the ability to exploit this previously unknown, differential gene amplification pattern for the purpose of diagnosing or classifying lung tumors of previously unknown pathology, which is not a "throw-away or insubstantial [use]." Appellants have asserted this utility based on the gene amplification data shown in Example 170; therefore no significant further research is required by the skilled artisan. Further, the data disclosed in the instant specification for the PRO341 gene are not preliminary. Based on the gene amplification data and the teachings in the Goddard Declaration, there is ample support for the Appellants' position that the PRO341 gene is a tumor marker for certain types of lung tumors. Thus, by providing a "reasonable use" for PRO341, Appellants respectfully submit that they have satisfied the "substantial utility" requirement for utility.

> The Examiner adds on page 3, citing the Hittelman reference for support that:
>
> "the literature reports that lung epithelium is at risk for cellular damage.....which result in aneuploidy before the epithelial cells turn cancerous".

Appellants agree. Hittelman studied premalignant lesions and suggests that epithelial tumors develop through a multistep process driven by genetic instability (see abstract). Hittelman showed that a subset of the same molecular changes found in associated tumor were also found in premalignant lesions, suggesting that these premalignant lesions might represent precursor lesions for associated tumors, i.e., a manifestation of a multistep tumorigenesis process. (See Hittelman, page 4, last three lines). Appellants therefore submit that, contrary to the Examiner's rejection, the Hittelman reference strongly supports the Appellants position that there is utility in identifying genetic biomarkers in epithelial tissues at cancer risk (also see Hittelman, abstract, line 4-7). Hittelman adds on page 2, fourth paragraph, line 3 that "it is important to identify

individuals at significantly increased cancer risk who might best benefit from different types of intervention". Taken together, even if, (which Appellants do not contend to) Appellants were to show that the observed PRO341 gene amplification were due to chromosomal aneuploidy, identifying genetic biomarkers like the PRO341 gene with this aneuploidy is a very important and useful step, according to Hittelman, in identifying individuals at significantly increased cancer risk. Therefore, Hittelman supports at least one utility for the PRO341 gene, that is, as a genetic biomarker for cancer or precancerous cells. As one skilled in the art would clearly know, early detection of lung cancer provides information in advance about risk assessment, prognosis and therapy for lung cancer.

Further, in the Advisory Action dated January 14, 2005, the Examiner adds (on page 2) that

> "the gene amplification assay (i)n the specification does not provide a comparison between the lung tumor samples and normal lung epithelium, and thus it is not clear that the PRO341 gene is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium."

Appellants strongly disagree. First of all, the specification clearly states that for controls, "tumor samples were tested in triplicates with Taqman™ primers and with internal controls, beta-actin and GADPH in order to quantitatively compare DNA levels between samples (page 548, lines 33-34). As a **negative control**, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 539, lines 27-29) and also, no-template controls (page 548, lines 33-34)." This protocol and the controls used therein are art accepted. Besides, the same gene amplification protocol and controls have been used to identify several other tumor markers for lung, colon, breast cancer etc. The art, and the USTPO has accepted this protocol and controls therein as credible and we have several allowed cases based on this very same protocol and control. The Examiner seems to be applying a heightened utility standard in this instance, which is legally incorrect.

Besides, Appellants showed that the gene encoding for PRO341 was significantly amplified 2.173 fold to 2.514-fold, in three lung tumors. These values are considered significant based on the Declaration by Dr. Audrey Goddard discussed above. By referring to the 2.173-fold to 2.514-fold amplification as "not clear" that is, whether the PRO341 gene is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium, the Examiner

appears to ignore the teachings within an expert's declaration without any basis, or without presenting any evidence to the contrary. Appellants respectfully draw the Examiner's attention to the Utility Examination Guidelines (Part IIB, 66 Fed. Reg. 1098 (2001)) which states that:

> "Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered".

Thus, barring evidence to the contrary, Appellants maintain that the fold amplification disclosed for the PRO341 gene is significant and forms the basis for the utility claimed herein.

Appellants add that they have shown significant DNA amplification in three out of the fourteen (3/14) lung tumor samples in Table 9A, Example 170 of the instant specification. The fact that 3/14 lung tumors tested positive in this study does not make the gene amplification data, by any means, less significant or spurious. As any skilled artisan in the field of oncology would easily appreciate, not all tumor markers are generally associated with every tumor, or even, with most tumors. In fact, some tumor markers are useful for identifying rare malignancies. That is, the association of the tumor marker with a particular type of tumor lesion may be rare, or, the occurrence of that particular kind of tumor lesion itself may be rare. In either event, even these rare tumor markers which do not give a positive hit for most common tumors, have great value in tumor diagnosis, and consequently, in tumor prognosis. The skilled artisan would certainly know that such tumor markers are very useful for better classification of tumors. Therefore, whether the PRO314 gene is amplified in three lung tumors or in most lung tumors is not relevant to its identification as a tumor marker, or its patentable utility. Rather, whether the amplification data for PRO341 is considered significant is what lends support to its usefulness as a tumor marker.

Thus, the Examiner has not established a *prima facie* case for lack of utility. Therefore, this rejection should be withdrawn based on consideration of the totality of evidence.

As a final note, Appellants submit that the utility presently asserted for the claimed invention meets the "substantiality" requirement set forth by the Utility Guidelines and required by the U.S. Supreme Court in Brenner v. Manson, 383 U.S. 519 (1966).

Hence, it is respectfully requested that that the outstanding rejection to Claims 124, 129-131 and 135-145 be reconsidered and that the rejection be reversed.

2. Claims 124, 129-131 and 135-145 also stand rejected under 35 U.S.C. §112, first paragraph since allegedly "the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well-established utility, one skilled in the art clearly would not know how to use the claimed invention."

Appellants respectfully traverse the rejection.

Based on the asserted utility for PRO341 in the diagnosis of certain types of lung carcinomas, the reduction to practice of the instantly claimed DNA sequence of SEQ ID NO: 19 in the present application (also see page 305) and the step-by-step disclosure of the gene amplification assay in Example 170, the skilled artisan would know exactly how to make and use the claimed nucleic acids for the diagnosis of lung carcinoma. Appellants submit that based on the detailed information presented in the specification and the advanced state of the art in oncology, the skilled artisan would have found such testing routine and not 'undue'.

Therefore, since the instantly claimed invention is supported by either a credible, specific and substantial asserted utility or a well-established utility, and since the present specification clearly teaches one skilled in the art "how to make and use" the claimed invention without undue experimentation, Appellants respectfully request reconsideration and reversal of this outstanding rejection to Claims 124, 129-131 and 135-145.

VIII. CONCLUSION

For the reasons given above, Appellants submit that present specification clearly describes, details and provides a patentable utility for the claimed invention. Moreover, it is respectfully submitted that based upon this disclosed patentable utility, the present specification clearly teaches "how to use" the presently claimed polypeptide. As such, Appellants respectfully request reconsideration and reversal of the outstanding rejection of claims 124, 129-131 and 135-145.

Respectfully submitted,

Date: July 26, 2005

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APPENDIX A

Claims on Appeal

124. An isolated nucleic acid comprising:

(a) the nucleic acid sequence of SEQ ID NO: 19;

(b) the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:19; or

(c) the full-length coding sequence of the cDNA deposited under ATCC accession number 209792.

129. The isolated nucleic acid of Claim 124 comprising the nucleic acid sequence of SEQ ID NO:19.

130. The isolated nucleic acid of Claim 124 comprising the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:19.

131. The isolated nucleic acid of Claim 124 comprising the full-length coding sequence of the cDNA deposited under ATCC accession number 209792.

135. A vector comprising the nucleic acid of Claim 124.

136. The vector of Claim 135, wherein said nucleic acid is operably linked to control sequences recognized by a host cell transformed with the vector.

137. A host cell comprising the vector of Claim 135.

138. The host cell of Claim 137, wherein said cell is a CHO cell, an *E. coli* or a yeast cell.

139. An isolated nucleic acid consisting of at least 30 nucleotide fragment of the nucleic acid sequence of SEQ ID NO: 19, or a complement thereof, that specifically hybridizes under stringent conditions to:

(a) the nucleic acid sequence of SEQ ID NO: 19 or a complement thereof;

(b) the full-length coding sequence of the cDNA deposited under ATCC accession number 209792 or a complement thereof;
wherein, said stringent conditions use 50% formamide, 5X SSC, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5X Denhardt's solution, sonicated salmon sperm DNA (50 μg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, and washes at 42°C in 0.2X SSC, at 55°C in 50% formamide followed by a high-stringency wash at 55°C in 0.1X SSC, EDTA; wherein said isolated nucleic acid molecule is suitable for use as a PCR primer or probe.

140. The isolated nucleic acid molecule of Claim 139 that is at least 50 nucleotides or above in length.

141. The isolated nucleic acid molecule of Claim 139 that is at least 60 nucleotides or above in length.

142. The isolated nucleic acid molecule of Claim 139 that is at least 70 nucleotides or above in length.

143. The isolated nucleic acid molecule of Claim 139 that is at least 80 nucleotides or above in length.

144. The isolated nucleic acid molecule of Claim 139 that is at least 90 nucleotides or above in length.

145. The isolated nucleic acid molecule of Claim 139 that is at least 100 nucleotides or above in length.